

In the Specification:

Please replace page 34 (comprising the previously filed Sequence Listing) with the substitute Sequence Listing submitted herewith. *Ins. B1 attach.*

At page 8, line 21, please delete "LRHR" and insert --LHRH--.

At page 17, line 32, please delete "L" and insert --F--. ?

At page 17, line 24, please delete "Ac-D-Nal-4-Cl-D-Phe-D-Pal-Ser-N-Me-Tyr-D-Asn-Leu-Lys(iPr)-Pro-Ala-NH₂" and insert --Ac-D-Nal-4-Cl-D-Phe-D-Pal-Ser-N-Me-Tyr-D-Asn-Leu-Lys(iPr)-Pro-D-Ala-NH₂--.

At page 17, line 27, please delete "Ac-D-Nal-4-Cl-D-Phe-D-Pal-Ser-Tyr-D-Asn-Leu-Lys(iPr)-Pro-Ala-NH₂" and insert --Ac-D-Nal-4-Cl-D-Phe-D-Pal-Ser-Tyr-D-Asn-Leu-Lys(iPr)-Pro-D-Ala-NH₂--.

At page 17, line 32, please delete "activity.In" and insert --activity. In--.

At page 32, line 3, please delete "clears" and insert --clear--.

At page 32, line 33, please delete "protions" and insert --portions--.

At page 33, line 12, please delete the second "the" at the end of the line.

In the Claims:

Please cancel claims 48-60.

Please add new claims 61-81.

B4 until
~~61.~~ 61. An LHRH antagonist comprising a peptide compound, wherein a residue of the peptide compound corresponding to the amino acid at position 6 of natural mammalian LHRH comprises a small polar moiety, wherein the peptide compound has LHRH antagonist activity, inhibits ovulation in at least 50% of treated rats in a standard rat antioviulatory assay at a dose of 5 µg/rat, and has an ED₅₀ for histamine release of at least 3 µg/ml, or a pharmaceutically acceptable salt thereof. *43*

62. The LHRH antagonist of claim 61, which inhibits ovulation in at least 50% of treated rats in a standard rat antioviulatory assay at a dose of 2 $\mu\text{g}/\text{rat}$.
63. The LHRH antagonist of claim 61, which inhibits ovulation in at least 50% of treated rats in a standard rat antioviulatory assay at a dose of 1 $\mu\text{g}/\text{rat}$.
64. The LHRH antagonist of claim 61, which has an ED_{50} for histamine release of at least 5 $\mu\text{g}/\text{ml}$.
65. The LHRH antagonist of claim 61, which has an ED_{50} for histamine release of at least 10 $\mu\text{g}/\text{ml}$.
66. The LHRH antagonist of claim 61, which is about 8 to about 12 residues in length.
67. The LHRH antagonist of claim 61, which is 9 to 11 residues in length.
68. The LHRH antagonist of claim 61, which is 10 residues in length.
69. The LHRH antagonist of claim 61, wherein the residue corresponding to the amino acid at position 6 of natural mammalian LHRH is selected from the group consisting of D-asparagine, D-threonine and D-glutamine.
70. The LHRH antagonist of claim 61, wherein the residue corresponding to the amino acid at position 6 of natural mammalian LHRH is D-asparagine.

71. A peptide compound comprising a structure:

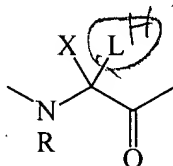
A-B-C-D-E-F-G-H-I-J (SEQ ID NO: 6)

wherein

A is pyro-Glu, Ac-D-Nal, Ac-D-Qal, Ac-Sar, or Ac-D-Pal;
B is His or 4-Cl-D-Phe;
C is Trp, D-Pal, D-Nal, L-Nal, D-Pal(N-O), or D-Trp;
D is Ser;

E is N-Me-Ala, Tyr, N-Me-Tyr, Ser, Lys(iPr), 4-Cl-Phe, His, Asn, Met, Ala, Arg or Ile;

F is



wherein

R and X are, independently, H or alkyl; and

L comprises a small polar moiety;

G is Leu or Trp;

H is Lys(iPr), Gln, Met, or Arg;

I is Pro; and

J is Gly-NH₂ or D-Ala-NH₂;

or a pharmaceutically acceptable salt thereof.

72. The peptide of claim 71, wherein F is selected from the group consisting of D-Asn, D-Gln, and D-Thr.

273. A peptide compound comprising a structure:

A-B-C-D-E-F-G-H-I-J

wherein

A is pyro-Glu, Ac-D-Nal, Ac-D-Qal, Ac-Sar, or Ac-D-Pal;

B is His or 4-Cl-D-Phe;

C is Trp, D-Pal, D-Nal, L-Nal-D-Pal(N-O), or D-Trp;

D is Ser;

E is N-Me-Ala, Tyr, N-Me-Tyr, Ser, Lys(iPr), 4-Cl-Phe, His, Asn, Met, Ala, Arg or Ile;

F is D-Asn;

G is Leu or Trp;

H is Lys(iPr), Gln, Met, or Arg;

I is Pro; and

J is Gly-NH₂ or D-Ala-NH₂;

or a pharmaceutically acceptable salt thereof.

44

3 74. A peptide compound comprising a structure:

✓ Ac-D-Nal-4-Cl-D-Phe-D-Pal-Ser-N-Me-Tyr-D-Asn-Leu-Lys(iPr)-Pro-D-Ala-NH₂;
or a pharmaceutically acceptable salt thereof.

4 75. A peptide compound comprising a structure:

Ac-D-Nal-4-Cl-D-Phe-D-Pal-Ser-Tyr-D-Asn-Leu-Lys(iPr)-Pro-D-Ala-NH₂;
or a pharmaceutically acceptable salt thereof.

76. A pharmaceutical composition comprising the peptide compound of claim 61, and
a pharmaceutically acceptable carrier.

77. A packaged formulation for treating a subject for a disorder associated with
LHRH activity, comprising the peptide compound of claim 61 packaged with instructions
for using the peptide compound for treating a subject having a disorder associated with
LHRH activity.

78. A method of inhibiting LHRH activity associated with a cell, comprising
contacting a cell with the peptide compound of claim 61, such that LHRH activity
associated with the cell inhibited.

79. The method of claim 78, wherein the cell is within a subject and the peptide
compound is administered to the subject.

80. A method of inhibiting growth of a hormone-dependent tumor in a subject,
comprising administering to a subject an effective amount of the peptide compound of
claim 61, such that growth of the hormone-dependent tumor in the subject is inhibited.

81. A method of inhibiting ovulation in a subject, comprising administering to a
subject an effective amount of the peptide compound of claim 61, such that ovulation in
the subject is inhibited.--